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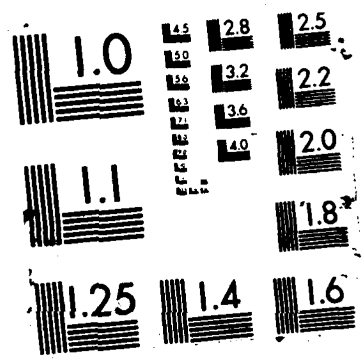
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This grant provided equipment for a multi-user, multi-tasking minicomputer (VAX 11-750) and a Dod funded research project (AFOSR-83-0335 and follow-on 87-0042) investigating the regulation of neurobiological responsiveness.

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DEPARTMENT OF DEFENSE

UNIVERSITY RESEARCH

INSTRUMENTATION PROGRAM

FINAL TECHNICAL/SCIENTIFIC REPORT

31 AUGUST, 1987

Submitted by:

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a. Abstract

This grant provided equipment for a multi-user, multi-tasking minicomputer (VAX 11-750) and a cluster of micro-computers (IBM-XT) to support a DoD funded This research project (AFOSR-83-0335 and follow-on 87-0042) investigat~~ing~~ed the regulation of neurobiological responsiveness.

High speed digitization of neurophysiological signals and their analysis were performed on-line using IBM-XT installed A-D conversions. In our research program we seek to determine how the phosphorylation state of identified brain proteins regulates inter-synaptic changes in communication between nerve cells, monitored electrophysiologically at the synapse using microelectrodes. The requested hardware provided the necessary computing power required to deal with the high data acquisition rate of brain potentials signalling synaptic change. In order to perserve an accurate representation of synaptic potentials the minmial storage capacity requirement for the data alone was 0.25-1.0 megabyte per daily individual experiment. We increase this requirement at the stage when we assessed interative experiments that tested the effect of specific phosphoprotein - manipulating chemical agents on synaptic potential change. The equipment purchased has been used in a series of studies (Routtenberg et al., 1985, 1986; Lovinger et al., 1985, 1986, 1987; Linden et al., 1986, 1987; Colley et al., 1987).

Our ability to rapidly collect and analyze electrophysiological data was a key factor in generating these studies in an efficient and coherent manner.

We have also written special programs to run densitometric analysis of brain phosphoproteins interfacing an E-C microdensitometer with an A/D board resident within the IBM-PC/XT.

b. Final Report: Supporting Information

The acquired instrumentation enhanced research currently funded by DoD (AIR FORCE - LIFE SCIENCES: AFOSR 87-0042); Principal Investigator - Aryeh Routtenberg). It provides an integrated and dedicated computing environment that has (a) sufficient power to operate on large data structures, (b) adequate speed to generate these structures on-line and (c) proven software to analyze these data structures in a multi-user environment.

Two valuable features of our current data handling and analysis are (1) the capacity to preserve the integrity of the original synaptic cpotential (2) the shipping of data to other, spreadsheet or statistical, programs without entering numerical values. With regard to the past point too often computational limitations require data reduction at the time of data collection, before analysis of potentials, leading to an inevitable consequent loss of information.

One principal target for the requested instrumentation has been the storage, retrieval and analysis of data structures generated by digitized neurophysiological signals. It is instructive to consider the rate at which such data are gathered. Such data are accumulated in the following fashion: a single 20 msec sample converted at a 100 KHz requires 2 Kbytes. To generate an I/O function requires at least 10 samples. To evaluate

synaptic reactivity before and after high frequency stimulation requires at least two such functions prior to stimulation and, evaluating the rate of decay of reactivity, 8 more functions. This 200 Kbyte chunk of information would then be directly compared to a similar data structure in which the effect of agents that modify protein phosphorylation would be tested using the exact same paradigm. Considering the effect of 4 different agents evaluated one time, as would occur using a 5-barreled micropipette, we have been looking at a total of 1 megabyte data storage. This is the minimal experimental protocol. Any additional information has required considerably more memory.

The DoD supported research for which the present instrumentation has been used is directed at the linkage between enhancement of synaptic reactivity <u>and</u> the phosphate content of particular identified brain proteins in the hippocampus. To study these proteins in this particular anatomical location, we pinpoint the locations along the septo-temporal hippocampal axis where synaptic invasion allows synaptic enhancement to occur.

We need to know the specific synaptic location on the dendrite where enhancement occurs. This enables us to evaluate the readjustments of the nerve cell over its entire receptive surface following enhancement. A recent report by Lovinger and Routtenberg (1987) used the computer for laminar profile analysis and current source density analysis. By on-line storage of such analyses we determined whether there were LTP-induced alterations in the laminar profile and the current source.

We have studied how alterations in synaptic reactivity are regulated by macromolecular structure. We have identified a particular phosphoprotein, Protein F1, which is directly related to alterations in Protein F1 phosphorylation. We have characterized the isoelectric point of F1 using two-dimensional gel electrophoresis (2D-GE). This is currently a powerful tool considerably enhancing our ability to understand the function and the subunit structure of Protein F1.

The computer instrumentation interfaces with existing data acquisition instrumentation within PI's laboratory. As this represents a computer installation in a somewhat sizable laboratory (circa 4500 sq.ft.) the major thrust of the hardware utilization has been directed toward interfacing with the current AFOSR supported research.

The VAX 11-750 has been used almost exclusively for the currently funded AFOSR project. No specific use by other groups within the university occurred as this was a dedicated installation.

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